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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,088	07/26/2001	Alessandro Lambiase	36226/125733	6075

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EXAMINER	
DI NOLA BARON, LILIANA	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,088	LAMBIASE, ALESSANDRO	
	Examiner	Art Unit	
	Liliana Di Nola-Baron	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of Applicant's request for continued examination and amendment, filed on November 20, 2003, is acknowledged.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Regarding claim 22, the limitation "retina" in line 3 renders the claim indefinite, because generic claim 21 reads on a method for the treatment of a pathology, excluding retinal pathologies. Thus, claim 22 fails to further limit the generic claim.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Louis (U.S. patent 5,641,750).

The patent provides a method for treating pathologies leading to vision loss comprising administering the neurotrophic factor GDNF (See col. 6, lines 5-20).

With regard to claim 13, 16 and 17, the patent includes inherited retinal degenerations, age-related macular degeneration, diabetic retinopathy and surgery-induced retinopathies among the pathologies treated by the method of the invention (See col. 6, line 55 to col. 7, line 3). The nerve growth factor claimed by Applicant is part of the neurotrophic factor family disclosed by the patent (See col. 1, line 55 to col. 2, line 65). With regard to the amount of nerve growth factor claimed by Applicant, the patent discloses an intraocular dose of 0.001-10 mg/day (See col. 20, lines 42-51). The patent does not specifically teach a dosage in microgram/ml, as claimed by Applicant, however, the patent teaches that the specific dose may be calculated by one of ordinary skill in the art in view of the body weight and organ size (See col. 20, lines 32-51). With regard to the limitation that the nerve growth factor passes through the external tissues to the internal tissues of the eye, the patent contemplates extraocular administration of the composition between the eyeball and the eyelid, as well as intraocular administration, and teaches the inclusion of an agent in topically applied ophthalmic compositions to promote the penetration or transport of the therapeutic agent into the eye (See col. 17, line 61 to col. 18, line 47).

With respect to claim 14, 18 and 19, the patent discloses formulations in the form of ophthalmic solutions, suspensions and ointments (See col. 17, lines 50-54).

Regarding claim 15, the patent provides ocular inserts, implants and sustained-release polymeric formulations (See col. 19, line 50 to col. 20, line 17).

With regard to claim 20, the patent discloses natural GDNF isolated from mammalian cells as well as recombinant GDNF (See col. 8, lines 9-62).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Louis to device a method for the treatment of a pathology affecting the internal tissues of the eye, comprising administering a nerve growth factor. The expected result would have been a successful method of treatment. Because of the teachings of Louis, that the ophthalmic compositions of the invention may be applied to treat retinal degenerations, one of ordinary skill in the art would have a reasonable expectation that the method claimed in the instant application would be successful in treating ocular disorders. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

6. Claims 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glaser et al. (U.S. Patent 5,767,079).

The patent discloses a method for the treatment of ophthalmic disorders, comprising administering a composition comprising nerve growth factor (See col. 8, lines 45-58 and col. 11, lines62-67).

With regard to claims 21-23, the patent includes disorders of the cornea and sclera, Sjogren's syndrome, an autoimmune disease, and corneal neovascularization due to trauma among the diseases treated by the method of the invention (See col. 8, line 54 to col. 9, line 18). The patent does not specifically teach that the nerve growth factor passes through the external tissues to the internal tissues of the eye, however, the patent teaches that the composition of the invention may be administered by different routes, including intraocular, subretinal, intrascleral and sub-conjuctival injection, depending on the nature and location of the pathology (See col. 10, lines 45-49). Thus, one of ordinary skill in the art would have been capable of determining the best route of administration into the eye, so that the active agent would reach the internal tissues of the eye.

With respect to claim 24, the patent does not specifically disclose the amount of nerve growth factor in the composition of the invention, however, the patent teaches that the formulations, method of administration and dosage depend upon the disorder to be treated and the history of the patient, and these factors are readily determinable during therapy (See col. 10, lines 25-35). Thus, one of ordinary skill in the art would have been able to determine the optimal dosage according to the disease to be treated and the condition of the patient.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Glaser et al. to device a method for the treatment of a pathology affecting the internal tissues of the eye, comprising administering a nerve growth factor. The expected result would have been a successful method of treatment. Because of the

teachings of Glaser et al., that ophthalmic compositions comprising nerve growth factors may be applied to treat ophthalmic disorders, including those affecting the cornea and sclera, one of ordinary skill in the art would have a reasonable expectation that the method claimed in the instant application would be successful in treating ocular disorders. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

7. Claims 25-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (U.S. Patent 5,641,749).

The patent provides a method for treating injury or degeneration of retinal ganglion cells comprising administering the neurotrophic factor GDNF (See col. 4, lines 55-67).

With regard to claim 25, 28, 29 and 33-36 the patent includes glaucoma associated with abnormalities within the optic nerve and characterized by loss of retinal ganglion cells, and secondary glaucoma caused by neovascularization or trauma, among the pathologies treated by the method of the invention (See col. 2, line 54 to col. 3, line 63). The nerve growth factor claimed by Applicant is part of the neurotrophic factor family disclosed by the patent (See col. 1, line 42 to col. 2, line 23). With regard to the amount of nerve growth factor claimed by Applicant, the patent teaches that the specific does may be calculated according to body weight and organ size, and is routinely made by those of ordinary skill in the art (See col. 18, line58 to col. 10). With regard to the limitation that the nerve growth factor passes through the external

tissues to the internal tissues of the eye, the patent contemplates extraocular administration of the composition between the eyeball and the eyelid, as well as intraocular administration, and teaches the inclusion of an agent in topically applied ophthalmic compositions to promote the penetration or transport of the therapeutic agent into the eye (See col. 16, line 17 to col. 17, line 42).

With respect to claims 26, 30 and 31, the patent discloses formulations in the form of ophthalmic solutions, suspensions and ointments (See col. 16, lines 6-10).

Regarding claim 27, the patent provides ocular inserts, implants and sustained-release polymeric formulations (See col. 18, lines 39-55).

With regard to claim 32, the patent discloses natural GDNF isolated from mammalian cells as well as recombinant GDNF (See col. 6, lines 38-51).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Yan et al. to device a method for the treatment of a pathology affecting the internal tissues of the eye, comprising administering a nerve growth factor. The expected result would have been a successful method of treatment. Because of the teachings of Yan et al., that the ophthalmic compositions of the invention may be applied to treat glaucoma, one of ordinary skill in the art would have a reasonable expectation that the method claimed in the instant application would be successful in treating ocular disorders. Therefore the

invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

8. Applicant's arguments, filed on November 20, 2003, have been fully considered and are persuasive in view of Applicant's amendment. Accordingly, the rejections of the previous Office action have been withdrawn.

Conclusion

9. Claims 13-36 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

December 23, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600